STATUS OF CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application.

Claims 1-6 **(canceled)**

Claim 7 **(currently amended)** The method according to claim ~~38, 40, 41, or 43~~38, 40, 41, 43, or 45, wherein said cellular component is selected from the group consisting of DNA, protein, and carbohydrate.

Claim 8 **(currently amended)** The method according to claim ~~38, 40, 41, or 43~~38, 40, 41, 43, or 45, wherein said RNase is encoded by a gene that is integrated into the genome of the cell producing the RNase.

Claim 9 **(currently amended)** The method according to claim ~~38, 40, 41, or 43~~38, 40, 41, 43, or 45, wherein said RNase is non-specific.

Claim 10 **(currently amended)** The method according to claim ~~38, 40, 41, or 43~~38, 40, 41, 43, or 45, wherein said RNase is RNase A, RNase M or RNase I.

Claim 11 **(currently amended)** The method according to claim ~~38, 40, 41, or 43~~38, 40, 41, 43, or 45, wherein expression of said RNase is transcriptionally, translationally, or post-translationally regulated.

Claim 12 **(currently amended)** The method according to claim ~~38, 40, 41, or 43~~38, 40, 41, 43, or 45, wherein said RNase is overproduced.

Claim 13 **(currently amended)** The method of according to claim ~~38, 40, 41, or 43~~ 40, 41, or 45, ~~,~~ wherein expression of said RNase is inducible.

Claim 14 **(currently amended)** The method according to claim ~~38, 40, 41, or 43~~40, 41, or 45, ~~,~~ wherein expression of said RNase is constitutive.

Claims 15-37 **(canceled)**

Claim 38 **(previously presented)** A method of preparing a substantially RNA-free cellular component comprising:

a) culturing a microbial cell producing said cellular component;

b) inducing the expression of an RNase in the cytoplasm of said cell in an amount sufficient to degrade substantially all of the RNA present;

c) lysing said cell; and

d) isolating said cellular component.

Claim 39 **(previously presented)** The method of claim 38 further comprising incubating said cell to allow said RNase to digest said RNA.

Claim 40 **(previously presented)** A method of preparing a substantially RNA-free cellular component comprising:

a) culturing a microbial cell producing the cellular component and an RNase, wherein said RNase is secreted into the periplasm of said cell;

b) lysing said cell to produce a cell lysate, wherein said cell lysate comprises said cellular component and sufficient RNase activity to degrade substantially all of the RNA present in said cell lysate;

c) incubating said cell lysate to allow said RNase to digest said RNA; and

d) isolating said cellular component.

Claim 41 **(previously presented)** A method of preparing a substantially RNA-free cellular component comprising:

a) culturing a microbial cell producing said cellular component and an RNase in a medium, wherein said cellular component and said RNase are secreted out of the cytoplasm of the cell into the medium and further wherein said medium contains sufficient RNase activity to degrade substantially all of the RNA present in said medium; and

b) isolating said cellular component.

Claim 42 **(previously presented)** The method of claim 41 further comprising incubating said medium to allow said RNase to digest said RNA.

Claim 43 **(currently amended)** A method of preparing a substantially RNA-free cellular component comprising:

a) culturing a microbial cell producing the cellular component ~~and an RNase~~, wherein said cellular component is secreted out of the cytoplasm of the cell;

b) inducing the expression of an RNase in the cytoplasm of said cell in an amount sufficient to degrade substantially all of the RNA present;

~~b)~~c lysing said cell to produce a cell lysate, wherein said cell lysate contains said cellular component and sufficient RNase activity to degrade substantially all of the RNA present in said cell lysate;

~~c)~~d) incubating said cell lysate to allow said RNase to digest said RNA; and

~~d)~~e) isolating said cellular component.

Claim 44 **(canceled)**

Claim 45 **(new)** A method of preparing a substantially RNA-free cellular component comprising:

a) culturing a microbial cell producing the cellular component and an RNase, wherein said cellular component is secreted out of the cytoplasm of the cell and said RNase is secreted into the periplasm of said cell;

b) lysing said cell to produce a cell lysate, wherein said cell lysate contains said cellular component and sufficient RNase activity to degrade substantially all of the RNA present in said cell lysate;

c) incubating said cell lysate to allow said RNase to digest said RNA; and

d) isolating said cellular component.

REMARKS

Claims 7-14 and 38-44 were pending. Claims 7-14 and 43 are amended herein. Claim 44 was canceled. Claim 45 is new. Claim 45 is, essentially, claim 44 rewritten in independent form following the amendment of claim 43 to recite that expression of the RNase is induced. Support for this amendment can be found, *inter alia*, on pages 34-39 of the application as filed.

The foregoing amendments reduce the number of issues. No new matter has been added.

Preliminarily, Applicants wish to thank Examiners Prouty and Ramirez for the very helpful interview conducted on September 16, 2003. As is evident from the Interview Summary, the only outstanding issue was the rejection for lack of enablement. The Examiners contended that the Zhu et al reference still brings into question whether or not RNase expressed in the cytoplasm will be active. The Examiners indicated that either a reference or experimental evidence, which contradicts Zhu et al, would be considered in overcoming this rejection.

Accordingly, Applicants direct the Examiner to Meador, et al, *Eur. J. Biochem.*, Vol. 187, pages 549-553, 1990 ("Meador et al,"copy enclosed), cited by the previous examiner, Examiner Tung, in the Final Rejection dated March 22, 2001 (copy enclosed). Meador et al reports that

> . . .RNase M was located only in the spheroplasts

and notes

> . . . it has been proposed that RNase M is the endonuclease for mRNA degradation in growing cells.

(Meador et al, page 549, abstract.) Later in the text, a 1989 paper by the same group is cited for the proposal – Cannistraro et al, *Eur. J. Biochem.*, vol. 181:363-370, 1989.

Meador et al also reports that *E. coli* mRNA from the lactose operon is preferentially cleaved between Pyd-Ado bonds, and that RNase M has a preference for Pyd-Ado bonds. (Meador et al, page 549, column 1, second full paragraph.) Meador et al further reports that the RNA of exponentially growing bacteria is degraded at about half the rate at which it is synthesized and propose that RNase M is the endonuclease that initiates mRNA degradation. (See Meador et al, page 552, col. 2, first full paragraph.)

Confirmation of the results presented by Meador et al showing that RNaseM is active in the cytoplasm can be found in Meador & Kennell, *Gene*, 95:1-7, 1990, also cited by the previous

Examiner, Examiner Tung, in the Rejection dated November 28, 2001 (copy enclosed). Meador & Kennell reports

> . . . RNase M is present in the cytoplasm and has a marked preference for cleavage of bonds between Y-A residues.

(Meador & Kennell, page 1, col. 2, first paragraph).

Applicants respectfully submit that the foregoing more than sufficiently contradicts the conclusion in Zhu et al that RNase in the cytoplasm is not active.

Conclusion

Applicants believe the claims are in condition for allowance. An early Notice of Allowance is therefore earnestly solicited. Applicants invite the Examiner to contact the undersigned at (215) 665-5593 to clarify any unresolved issues raised by this response.

Respectfully submitted,

Date: October 2, 2003

Doreen Yatko Trujillo
Registration No. 35,719

COZEN O'CONNOR, P.C.
1900 Market Street, 6th Floor
Philadelphia, PA 19103-3508
(215) 665-5593 - Telephone
(215) 701-2005 - Facsimile